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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

Date: November 30, 2011

MEMORANDUM

SUBJECT: **Tebuconazole:** Human Health Risk Assessment for Proposed Use on Almond, Apple, Cherry, Peanut, Pecan, Pistachio, Tree Nuts, Watermelon, and Wine Grapes.

PC Code: 128997
Decision No.: 402626
Petition No.: NA
Risk Assessment Type: Single Chemical/ Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D387596, D385877
Registration No.: 264-752
Regulatory Action: Section 3
Case No.: NA

CAS No.: 107534-96-3
40 CFR: §180.474

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Introduction

Bayer CropScience (Bayer) is requesting a Section 3 registration for the proposed use of the active ingredient tebuconazole on almond, apple, cherry, peanut, pecan, pistachio, tree nuts, watermelon, and wine grapes. The Registration Division (RD) requested that the Health Effects Division (HED) evaluate toxicology and residue chemistry data and conduct dietary and aggregate exposure and risk assessments, as needed, to estimate the risk to human health that will result from these new tolerances.

The proposed label LUNA® EXPERIENCE (EPA Reg. No. 264-1091) contains 1.67 lb per

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gallon of product of each of the active ingredients tebuconazole and fluopyram. In a separate risk assessment document (DP385636, S. Healy, 11/30/11) HED assessed the proposed use of fluopyram on a variety of agricultural food crops, including almond, apple, cherry, peanut, pecan, pistachio, tree nuts, watermelon, and wine grapes. The LUNA® EXPERIENCE label proposes foliar applications by ground, aerial, airblast, and chemigation methods. Additionally, applications in greenhouses are proposed for watermelons. The proposed label is summarized in Table 1.

TABLE 1. Use Profile for LUNA® EXPERIENCE (EPA Reg. No. 264-1091).

Crop[1]	Target of Application	Application Equipment	Maximum Single Application Rate (lb ai/A)	Re-Treatment Interval (days)	Preharvest Interval (days)	Maximum Seasonal Application Rate (lb ai/A)	Applications per Season
Almond	Foliar	Aerial, Chemigation, Airblast	0.222	7-14	35	0.444	NS[1]
Apple	Foliar	Chemigation, Airblast	0.130	7-14	75	0.444	NS
Cherry	Foliar	Aerial, Chemigation, Airblast	0.0926	7-14	0	0.184	NS
Peanut	Foliar	Aerial, Chemigation, Groundboom	0.205	14	14	0.444	NS
Pecan	Foliar	Aerial, Chemigation, Airblast	0.222	14	AS[2]	0.444	NS
Pistachio	Foliar	Aerial, Chemigation, Airblast	0.222	10-14	35	0.444	NS
Tree Nuts[3]	Foliar	Aerial, Chemigation, Airblast	0.222	7-21	35	0.444	NS
Watermelon (field)	Foliar	Chemigation, Groundboom	0.222	10-14	7	0.444	NS
Watermelon (greenhouse)	Foliar	Chemigation, Groundboom, Handwand, Backpack	0.222	10-14	7	0.444	NS
Wine Grapes	Foliar	Chemigation, Groundboom, Airblast	0.112	12-21	14	0.444	NS

1 Not specified.
2 Do not apply after shucks begin to split.
3 Tree nuts includes: beech nut, brazil nut, cashew, chestnut, chinquapin, filbert (hazelnut), hickory nut, macadamia nut (bush nut), walnut (including black and English (Persian) walnuts).

Tebuconazole is a triazole fungicide currently registered for disease control on a variety of fruit and field crops. The triazoles act by inhibiting C14-demethylase, an enzyme which plays a role in sterol production in fungi. The use of tebuconazole on almond, apple, cherry, peanut, pecan, pistachio, tree nuts, watermelon, and wine grapes were previously assessed by HED (see DP315464, B.O'Keefe, 4/16/08 and DP352188, S. Winfield, 4/30/08); and these crops appear on the registered Elite® 45 DF Fungicide (EPA Reg. No. 264-749) or Folicur® 3.6 F Foliar Fungicide (EPA Reg. No. 264-752) labels all at maximum single application rates equal to or greater than the proposed rates on the LUNA® EXPERIENCE label. Retreatment intervals and preharvest intervals for these crops are the same, or longer, on the LUNA® EXPERIENCE label. Maximum seasonal application rates on the LUNA® EXPERIENCE label are the same or lower than those on the Elite® 45 DF Fungicide or Folicur® 3.6 F Foliar Fungicide labels. In the previous HED assessments dietary and aggregate risk estimates did not exceed HED's level of concern for use on almond, apple, cherry, peanut, pecan, pistachio, tree nuts, watermelon, and

wine grapes. Given the very similar proposed use patterns for these crops on the LUNA® EXPERIENCE label, HED does not expect dietary or aggregate risk estimates to exceed HED's level of concern for tebuconazole on these crops.

HED notes that although the use patterns listed on the proposed LUNA® EXPERIENCE label are very similar to those already assessed for tebuconazole that the risk estimates for occupational handlers and post-application workers would not be exactly the same as previously assessed, because of recent HED changes to occupational handler unit exposure values and transfer coefficients for post-application assessments. Therefore, these occupational handler and post-application worker exposures are assessed here.

Toxicity Endpoint and Point of Departure Selections

The toxicity endpoints and points of departure established for tebuconazole have been re-evaluated in conjunction with each new use application according to the current policy, newly available data, and any changes in the exposure scenario. At this time, the toxicity endpoints and points of departure previously selected for risk assessment (DP256074 and DP276447, S Winfield, 04/18/08) are valid and will be employed for this risk assessment. A full discussion of the endpoints selected for risk assessment may be found in the above referenced risk assessment. The summary of toxicity endpoints and points of departure are presented in Table 2.

Table 2. Summary of Toxicological Doses and Endpoints for Tebuconazole for Use in Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Short-/Intermediate-Term (1-30 days/1-6 months)	LOAEL=8.8 mg/kg/day	UF_A=10x UF_H=10x UF_L=3x DAF = 23.1%	Occupational LOC for MOE =300	Developmental Neurotoxicity Study - Rat. LOAEL = 8.8 mg/kg/day based on decreases in body weights, absolute brain weights, brain measurements and motor activity in offspring.
Inhalation Short-/Intermediate-Term (1-30 days/1-6 months)	LOAEL=8.8 mg/kg/day	UF_A=10x UF_H=10x UF_L=3x	Occupational LOC for MOE =300	Developmental Neurotoxicity Study - Rat. LOAEL = 8.8 mg/kg/day based on decreases in body weights, absolute brain weights, brain measurements and motor activity in offspring.
Cancer (oral, dermal, inhalation)	Classification: Group C- possible human carcinogen based on statistically significant increase in the incidence of hepatocellular adenoma, carcinoma, and combined adenoma/carcinomas in both sexes of NMRI mice. The chronic risk assessment is considered to be protective of any cancer effects; therefore, a separate quantitative cancer risk assessment is not required.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key date (i.e., lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable. DAF = dermal absorption factor.

Occupational Handler Exposure and Risk

No chemical-specific handler exposure data were submitted in support of this Section 3 registration. To assess handler exposures for regulatory actions when chemical-specific monitoring data are not available, HED relies on the most scientifically-reliable surrogate data

currently available from various sources such as the Pesticide Handler Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), and the Outdoor Residential Exposure Task Force (ORETF). Some of this data, such as the industry task force data, is compensatory, subject to the data protection provisions of FIFRA. HED policy on use of surrogate data is described in more detail on the Agency's website (http://www.epa.gov/pesticides/science/handler-exposure-data.html). Scenario-specific surrogate exposure data, including their sources, are presented in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (http://www.epa.gov/pesticides/science/handler-exposure-table.pdf). HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure.

Non-cancer short- and intermediate-term occupational handler exposures and risk estimates are shown in Table 3. Risk estimates for combined dermal (with gloves) and inhalation exposures all resulted in MOEs ≥300, and therefore, do not exceed HED's level of concern.

Table 3. MOEs for Occupational Handlers of Tebuconazole.

Exposure Scenario	Crops	Dermal Unit Exposure (mg/lb ai) [1]	Inhalation Unit Exposure (mg/lb ai) [2]	Maximum Application Rate (lb ai/A) [3]	Amount Treated (A/day) [4]	Short-/Int-term Combined MOE [5]
Mixer/Loader						
Mixing/Loading Liquid (open pour) for Groundboom application	Peanut	0.0376 (with gloves)	0.000219	0.2048	80	3,600
	Watermelon	0.0376 (with gloves)	0.000219	0.2218	80	3,300
	Wine Grapes	0.0376 (with gloves)	0.000219	0.1122	80	5,400
Mixing/Loading Liquid (open pour) for Chemigation or Aerial application	Peanut	0.0376 (with gloves)	0.000219	0.2048	350	830
	Watermelon	0.0376 (with gloves)	0.000219	0.2218	350	760
	Wine Grapes	0.0376 (with gloves)	0.000219	0.1122	350	1,500
Mixing/Loading Liquid (open pour) for Airblast application	Cherry	0.0376 (with gloves)	0.000219	0.0926	40	16,000
	Apple	0.0376 (with gloves)	0.000219	0.1304	40	11,000
	Almond, Pecan, Pistachio, Tree Nuts	0.0376 (with gloves)	0.000219	0.2218	40	6,700
Applicator						
Groundboom application	Peanut	0.0161 (with gloves)	0.00034	0.2048	80	7,900
	Watermelon	0.0161 (with gloves)	0.00034	0.2218	80	7,300
	Wine Grapes	0.0161 (with gloves)	0.00034	0.1122	80	14,000
Aerial application (Enclosed	Peanut	0.0050	0.000068	0.2048	350	6,000

Table 3. MOEs for Occupational Handlers of Tebuconazole.						
Exposure Scenario	**Crops**	**Dermal Unit Exposure (mg/lb ai) [1]**	**Inhalation Unit Exposure (mg/lb ai) [2]**	**Maximum Application Rate (lb ai/A) [3]**	**Amount Treated (A/day) [4]**	**Short-/Int-term Combined MOE [5]**
Cockpit)	Watermelon	0.0050	0.000068	0.2218	350	5,600
	Wine Grapes	0.0050	0.000068	0.1122	350	11,000
Airblast application (Open Cab)	Cherry	0.36	0.0045	0.0926	40	1,600
	Apple	0.36	0.0045	0.1304	40	1,200
	Almond, Pecan, Pistachio, Tree Nuts	0.36	0.0045	0.2218	40	680
Flagger						
Flagging for Aerial application	Peanut	0.011	0.00035	0.2048	350	2,500
	Watermelon	0.011	0.00035	0.2218	350	2,400
	Wine Grapes	0.011	0.00035	0.1122	350	4,700

[1] Dermal unit exposure values represent baseline clothing (long pants, long sleeved shirts, shoes, and socks), except where the addition of gloves is indicated.
[2] Inhalation unit exposure values represent no respirator.
[3] Application rates are based on maximum proposed values.
[4] Amount treated is the area that can be reasonably applied in a single day for each exposure scenario of concern, based on the application method and formulation/packaging type. (Standard EPA/OPP/HED values).
[5] Short-/Intermediate-Term Combined MOE = LOAEL (8.8 mg/kg/day) / [Daily Absorbed Short-/Intermediate-Term Dermal + Short-/Intermediate-Term Inhalation Dose]. The LOC is 300. Daily Absorbed Dermal Dose (mg/kg/day) = [Dermal unit exposure * 23.1% (Dermal absorption) * Application rate * Area treated] / 60-kg Body weight. Daily Absorbed Inhalation Dose (mg/kg/day) = [Inhalation unit exposure * 100% (Inhalation absorption) * Application rate * Area treated] / 60-kg Body weight.

Occupational Post-Application Exposure and Risk Estimales

Occupational post-application exposure can occur via the dermal and/or inhalation routes. Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for tebuconazole at this time primarily because of the low vapor pressure (9.8 x 10^{-9} mm Hg (20°C)) and the low proposed use rates (0.0926 to 0.2218 lb ai/A). However, there are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency is in the process of evaluating the SAP report as well as available post-application inhalation exposure data generated by the Agricultural Reentry Task Force and may, as appropriate, develop policies and procedures, to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for tebuconazole.

Proposed uses include applications in greenhouses. The WPS for Agricultural Pesticides contains requirements for protecting workers and bystanders from inhalation exposures during

and after greenhouse applications through the use of ventilation requirements. For these reasons, post-application inhalation exposures and risks were not quantitatively assessed for the proposed greenhouse uses.

Since, there is the possibility for agricultural workers to have post-application dermal exposure to tebuconazole following its proposed agricultural crop uses, occupational post-application short- and intermediate-term dermal exposure and risks were assessed.

No post-application data were submitted in support of this registration action; therefore, dermal exposures during post-application activities were estimated for the various tasks that post-application workers might perform on each crop grouping using dermal transfer coefficients from the Science Advisory Council for Exposure Policy Number 3 (http://www.epa.gov/pesticides/science/exposac_policy3.pdf). This policy reflects adoption of all Agricultural Re-Entry Task Force (ARTF) data. Use of the data in this policy requires compensation to the ARTF under FIFRA. The transfer coefficients (TCs) used in this assessment were taken from the Agency's revised Agricultural Transfer Coefficient SOP. Many of the TCs in this SOP are based on work of the ARTF.

The post-application exposure associated with the proposed agricultural crops is summarized in Table 4. The occupational post-application MOEs for almond, cherry, peanut, pecan, pistachio, tree nuts, and watermelon do not exceed HED's level of concern (MOEs ≥300) with dermal MOEs ranging from 300 to 990. However, an MOE ≥300 is not achieved until day 1 after treatment for apple and day 10 after treatment for wine grapes. Therefore, for almond, cherry, peanut, pecan, pistachio, tree nuts, and watermelon the restricted entry interval (REI) is based on the acute toxicity of tebuconazole technical material. Tebuconazole is classified as toxicity category III by the dermal route of exposure and for eye irritation potential and category IV for skin irritation potential. Under the Worker Protection Standard for Agricultural Pesticides, active ingredients classified as acute toxicity categories III or IV for these routes are assigned a 12-hour REI. Therefore, the 12-hour REI that appears on the proposed label is adequate for almond, cherry, peanut, pecan, pistachio, tree nuts, and watermelon. However, for apple a 1 day REI is required and for wine grapes a 10 day REI is required.

Table 4. Exposure and Risk Assessment for Tebuconazole for Occupational Postapplication Activities

Crops (PHI)	Maximum Application Rate (lb ai/A)	Dermal Transfer Coefficient (cm^2/hr) (Activities)	Days After Treatment (days)	Dislodgeable Foliar Residue (DFR)[1] (µg/cm^2)	Daily Dose[2] (mg/kg/day)	Short- & Intermediate-Term Dermal MOE[3]
Watermelon	0.2218	1900 (irrigation by hand set)	0	0.4974	0.0291	300
Apple	0.1304	3600 (thinning fruit)	0	0.2925	0.0324	**270**
			1	0.2632	0.0292	300
Peanut	0.2048	1900 (irrigation)	0	0.4593	0.0269	330
Cherry	0.0926	3600 (thinning fruit)	0	0.2077	0.0230	380
Wine Grape	0.1122	10100 (leaf pulling, tying/training)	0	0.2516	0.0783	**110**
			9	0.0975	0.0303	**290**
			10	0.0877	0.0273	320
Almond	0.2218	580 (scouting)	0	0.4974	0.0089	990

Table 4. Exposure and Risk Assessment for Tebuconazole for Occupational Postapplication Activities

Crops (PHI)	Maximum Application Rate (lb ai/A)	Dermal Transfer Coefficient (cm^2/hr) (Activities)	Days After Treatment (days)	Dislodgeable Foliar Residue (DFR)[1] (µg/cm^2)	Daily Dose[2] (mg/kg/day)	Short- & Intermediate-Term Dermal MOE[3]
Pecan	0.2218	580 (scouting, hand pruning)	0	0.4974	0.0089	990
Pistachio	0.2218	1400 (hand harvesting)	0	0.4974	0.0214	410
Tree Nuts	0.2218	1400 (hand harvesting)	0	0.4974	0.0214	410

[1] DFR = Application Rate (lb ai/A) x 4.54E+8 µg/lb x 2.47E-8 A/cm^2 x Percent Residue Available Day 0 (20%)
[2] Daily Dose = [DFR x (0.001 mg/µg) x Dermal Transfer Coefficient x Dermal Absorption Factor (23%) x Exposure Time (8 hr)] / [Body weight (60 kg)]
[3] MOE = LOAEL/Daily Dose. Short-/Intermediate-Term LOAEL = 8.8 mg/kg/day.

Conclusions

The proposed use pattern of tebuconazole (co-formulated with fluopyram in LUNA® EXPERIENCE) on almond, apple, cherry, peanut, pecan, pistachio, tree nuts, watermelon, and wine grapes is very similar to uses that have already been assessed. Therefore, the registration of this product will not alter the aggregate human health risk assessment for tebuconazole. However, due to recent changes in how HED calculates post-application risk estimates the use of this proposed product on apple and wine grapes results in risk estimates that will require REIs of 1 and 10 days, respectively. The registration of the LUNA® EXPERIENCE product on almond, cherry, peanut, pecan, pistachio, tree nuts, and watermelon will not result in any risk estimates of concern.

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